PATENT SPECIFICATION (11) 1444024

1444024

(21) Application No. 34785/73 (22) Filed 20 July 1973
(44) Complete Specification published 28 July 1976
(51) INT CL² A61K 33/04 31/095 31/195 31/19 31/355 37/02
(52) Index at acceptance
A5B 201 20Y 244 246 24X 24Y 275 27Y 281 284 285 28Y 311 313 314 315 317 31X 31Y 362 364 365 36X 36Y 381 38Y 392 39X 401 402 403 404 405 40Y 410 411 41X 41Y 481 482 483 486 48Y 491 49Y 551 556 55Y 576 57Y 586 58Y 616 61Y 641 643 64Y 77Y

(19) 

(54) FOOD AND FEED SUPPLEMENTS

(71) I, RICHARD ALBERT PASSWATER, a citizen of the United States of America, of 529 Southview Avenue, Silver Spring, State of Maryland, United States of America, do hereby declare the invention for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to food and feed supplements. More particularly this invention is related to feed and food supplements which are effective in preventing the occurrence and/or retarding of all types of cancer.

Separatum Experientia 26, 840 (1970), "Vitamin E Deficiency and Chemical Carcinogenesis", states:

"Since vitamin E and intracellular antioxidants are reported to be enriched in tumor tissues as compared to normal tissue, some retardation of tumor induction of tumor growth might be expected in acute vitamin E deficiency. Since the growth of the animals in group 4 was poor, it was difficult to ascribe the decreased size of liver tumors observed in several rats from this group to vitamin E deficiency alone. Surprisingly, Swick and Baumann have reported that dietary vitamin E decreased the incidence of hepatomas when large amounts of the vitamin were fed after administration of 3-methyl-4 dimethylamino-azobenzene.

"Miller et al. used a diet containing 0.06%, p-dimethyl-aminoazobenzene and low in vitamin E and have concluded that vitamin E does not exert any effect on the carcinogenicity of p-dimethylaminoazobenzene. Since they used relatively larger rats (initial wt, 180 g vs 60 g used in the present experiment) a lower level of fat (5% vs 10%), a much shorter total period of experimentation (6 months vs 18 months), and did not establish the vitamin E deficiency status of their rats, their conclusion may perhaps be questioned. However, the present results, obtained with a different carcinogen (FAA) under more controlled conditions are essentially in agreement with their data. Thus, it can be stated that vitamin E deficiency, under the present experimental conditions, does not accelerate the induction or growth of tumors by FAA in rats." [Emphasis supplied] [col. 2 2nd and 3rd paragraphs].

So it is seen that the Separatum E reference discloses that a deficiency of Vitamin E does not accelerate the induction of cancer.

Brewer, Keith A., "Excitation of the Hydrogen Double Bond" America Scientist, Vol. 56, No. 3, at pages 261 and 263, states that cancer can be induced in the skin by exposure to ultraviolet radiation by penetrating radiation and by long exposure to heat. It also states that carcinogens are complex molecules containing benzene rings with substitutions in the meta position and such compounds can be synthesized from polymers upon excitation by heat, UV radiation, x-rays, α, β and γ rays and electron bombardments.

Webster, James "Vitamin C—The Protective Vitamin", Universal-Award House, Inc., (1971) at pages 61 to 64, 154 and 155, deals with vitamin C (ascorbic acid) and cancer. After referring to an article published in the June 21, 1968, issue of "Medical World News", it stated: "*** Dr. *** advises his patients who have had bladder cancer that the trouble *may* not come back if they take lots of Vitamin C". [Emphasis supplied] [at page 61, last four lines]. That statement is only speculative as it uses the word "may". It is also noted that that statement only deals with using Vitamin C after they have already had bladder cancer. The reference quotes: "He prescribes a gram and a half a day to prevent recurrences of carcinomia of the bladder" [at page 62, lines 3 and 4]. Any positive aspects of that statement is eliminated by the following further quotation: '"We have enough circumstantial evidence to warrant a trial of ascorbic acid to prevent recurrences"' [emphasis supplied] [at page 62, lines 1 0and 11]. That state-

ment, at best, is only an invitation to experiment.

The *Webster* reference, in dealing with the Medical World News Article, also quotes:

> "The Tulane researches could not demonstrate significant differences in the 24-hour excretion of 3-HOA by bladder tumor patients, smokers and normal patients who were nonsmokers. But they did find much more cinnabaric acid in urine from the tumor patients. And in all three groups, ascorbic acid prevented the formation of this compound." [At page 63, lines 14 to 20.]

That is not a statement that large amounts, i.e., 1.5 grams of ascorbic acid will prevent or cure any type of cancer.

The Webster reference, at page 66, lines 9 to 13, stated: "*** the efficiency of Vitamin C *** except for hopeful results concerning bladder cancer." [Emphasis supplied.] That statement is only speculative and, at best, an invitation to experiment.

The Webster reference, in dealing with an article by E. Schneider in the A.M.A. Journal quoted: "'A Vitamin C deficiency varying from 3000 to 9000 mg, with an average deficiency of 4550 mg was revealed by serial examination with the saturation method performed on ten patients with carcinoma of the stomach, rectum, and uterine cervix and with bronchial carcinoma. In an attempt at improving the general condition of patients with carcinoma before surgical intervention, this Vitamin C deficiency was compensated by daily administration of 1000 to 2000 mg of Vitamin C. Administration of Vitamin C increases the . . . defense power but does not exert any anticancerous effect'.' [At page 154, lines 10 to 20.] That statement only states that the "defense power" whatever that means is increased and does not state that large amounts of Vitamin C prevent cancer. The phrase "defense power" most likely applies to the normal body defense mechanisms against colds and normal diseases because of the reference of giving the large amounts of Vitamin C in "an attempt at improving the general condition of patients with carcinoma before surgical intervention".

The Webster reference, in continuing on the Schneider article, quotes a passage that states that daily dosages of 1000 mg. of Vitamin C and large amounts of Vitamin A to various cancer patients helped their general condition, prolonged life and temporarily reduced the size of tumors. Whatever that quotation contains, it does not state that large amounts of Vitamin C prevents cancer formation. A further quotation summarizes the entire disclosure in perfect fashion: "'*Massive vitamin therapy has the advantage of being free of any risk, since it has no component that may potentially influence tumor development*'." [Emphasis supplied] [at page 155, lines 20 to 22.] That is another way of saying that high dosages of Vitamin C or Vitamins C and A are not potential means for preventing the development of cancer.

Georgieff, K. K., "Free Radical Inhibitory Effect of Some Anticancer Compounds", Science, Vol. 173, No. 3996 (1971), pp. 537 to 539, was in attempt to determine whether some typical anticancer compounds were also free radical inhibitors that might block biological reactions involving free radicals. The *Georgieff* reference, in Table I, shows that at least n-propyl gallate, Mitomycin C, hydroxyurea and Vitamin A alcohol have higher free radical inhibition factors than does Vitamin C. Copper compounds are also better. Vitamin C is stated to have little or no anti-tumor activity, but it is supported to potentiate the activity of other anti-cancer compounds. The *Georgieff* reference states: "Vitamin C ***. *** can act as a reducing agent in redox polymerization systems. Thus, under one set of conditions, L-ascorbic acid can promote the formation of unstable free radicals and under another it can inhibit them. *** Ascorbic acid *** appears to inhibit various tumors. Glycolysis and respiration of the tumor cells are diminished. [At page 539, col. 1, line 21 to 53.] That statement is speculative and shows that known L-ascorbic acid action is confusing and contradictory. The further speculative nature of the *Georgieff* reference is shown by the following quotation: "Several ubitiquitous compounds (copper vitamins A and C, and ketoaldehydes), which either suppress the growth of cancer or enhance the carcinocidal effect of other anticancer compounds, show substantial free radical inhibition. Many other natural compounds also appear to be free radical inhibitors as a result of their chemical structures. Most synthetic anticancer compounds that I studied displayed significant inhibitory activity. Thus, free radical inhibitors would appear to play some important role in the biochemistry of the normal cell and in the suppression of cancerous growth." [At page 539, col. 2, lines 8 to 23.]

The theory behind the speculations in the *Georgieff* reference is stated to be "Previous investigators have found that free radicals are formed when living tissue is irradiated with high energy radiation, and when the dose is sufficiently high, carcinogenesis occurs. The host is often protected with free radical scavengers when being treated with radiation. *** the exact role of these free radicals has not yet been established. These observations, as well as those in previous paragraphs, are consistent with the hypothesis that in normal cells there is a balance between unstable free

radicals and free radical inhibitors (and their resulting stable free radicals), which probably involves several or many different reactions. An excess of unstable free radicals will tend to induce reactions that will result in carcinogenesis, whereas free radical inhibitors will tend to restore the balance and inhibit cancer. If this hypothesis is correct, the addition of adequate amounts of certain nontoxic free radical inhibitors to the human diet may reduce the incidence of some types of cancer." [Emphasis supplied] [at p 539 col. 2, line 36 to col. 3, line 12]. Even the *Georgieff* reference states: "Whether my inhibition factors *** have any quantitative significance in biological systems has yet to be established". [At p. 537, col. 2, line 47, to col. 3, line 2] suggests the use of very low amounts free radical inhibitors for biological systems.

Feedstuffs, "The Case for Selenite As a Feed Additive", vol. 43, No. 13, p. 12 et seq., states that Se was long ago alleged to be a possible cause of cancer, but speculates that a deficiency of Se or vitamin E may reduce resistance to carcinogen attack.

Feedstuffs, April 17, 1971, Letters To The Editor, page 10, First Letter, states "*** Dr. R. J. Shamberger's discovery of inhibition of experimental skin carcinogenesis in mice by simultaneous skin painting with sodium selenide or vitamin E and croton oil ***." It also states that there is an inverse relationship between human cancer mortality and the geographic distribution of Se.

Can. Med. Ass. J., Vol. 100, April 12, 1969, Correspondence page 682, Shamberger Letter, disclosed sodium selenide reduced the number of animals with tumors in several carcinogenesis experiments; likewise with animals fed adequate selenium levels. It also states that there is an inverse relationship between selenium blood levels and human cancer death rates.

The Merck Index, 6th Ed., 1962, page 626, states that methionine is a nutrient, that the recommended daily intake of L-methionine for a normal adult male is 2.2 grams, has been used in fatty infiltration, cirrhosis of the liver and toxic hepatitis, that anorexia nausea and vomiting may occur following large doses, and the oral dosage of DL-methionine was 3 to 6 groups per day.

Chem & E. News, April 10, 1972, p. 14, essentially teaches that cancer produces or puts out free radicals.

In Harman Denham, "Free Radical Theory of Aging: Effect of Free Radical Reaction Inhibitors on the Mortality Rate of Male LAF_2 Mice," J. of Gerontology, Vol. 23, No. 4, Oct. 1968, at page 478 it was reported that no gross tumors were found in mice during an experimental period in which they were fed a daily diet which contained among other things, 20 mg. of α-tocopherol acetate.

C & EN, June 29, 1970, "Vitamin A and E Help Maintain Lung Health", states that in one study high doses of vitamin A, given to benzpyrene-treated hamsters, can inhibit completely the appearance of squamous tumors of the lung. Also, in another study, healthy hamsters, which had been given large dosages of vitamin A for 12 days, had benzpyrene-induced anaplastic tumors from the lungs of hamsters transplanted. It was stated that it was not known from those tests whether there might be a change in cell structure and tumor growth rate.

Harman, Denham, "Prolongation of life: Role of Free Radical Reactions In Aging", J. of the American Geriatrics Society, Aug. 1969 at page 728 treats the subject of cancer in the title area. *Harmon*, at page 728, lines 13 to 21 states:

> "Recently it has been observed that the incidence of mammary carcinoma induced in female white rats by 7,12-dimethyl benz(a) anthracene was higher when the diet contained 20 per cent by weight of corn oil in comparison to the same amount of a saturated fat, coconut oil (31). This result probably is a reflection of a higher rate of lipid peroxidation in the rats fed the corn oil diet, since in a similar experiment in which the base diet was 20 per cent by weight of corn oil to which was added either 5 or 20 mg of α-tocopherol acetate per 100 grams of diet, the rats receiving the vitamin-E supplemental diet had significantly fewer tumors (32)."

It is noted that the quotation is directed to showing that a corn oil diet is probably the key to the lowering of the occurrence of tumors and mammary carcinoma.

Mirvish, Sidney S., et al., "Ascorbate-Nitrate Reaction: Possible Means of Blocking the Formation of Carcinogenic N-Nitroso Compounds," Science, Vol. 177, July 7, 1972, at pages 65 to 68, presents chemical data that shows that ascorbic acid blocks the formation of carcinogenic N-nitrose compounds by the chemical reaction between nitrous acid and compounds piperazine. Urea and ammonium sulfamate were less effective blocking agents. The article suggested the possibility of invivo formation of carcinogenic N-nitroso compounds from drugs could be lessened by the combination of such drugs with ascorbic acid. The article states "that ascorbic acid

might be used for this purpose." [Emphasis supplied.]

Most animals synthesize enough vitamin C for their need, but man and other primates do not have the capacity to synthesize vitamin C.

The present invention may provide food and feed supplements which are effective in preventing the occurrence and retarding of all types of cancer.

The food and feed supplement of the invention contains as essential ingredients (a) an edible antioxidant selected from vitamin E, vitamin C, other edible natural antioxidants, edible synthetic antioxidants and mixtures thereof, (b) an edible sulfur-containing amino acid, an edible sulfur-containing peptide, an edible sulfur-containing protein or mixtures thereof and (c) edible selenium as a selenium oxide or an organic selenium compound. Hereinafter the term "edible sulfur-containing ingredient" encompasses the various substances listed in (b) just above. The supplement contains enough of the edible sulfur-containing ingredients for consumption of from 100 milligrams to 5 grams thereof per 120 pounds of body weight per day. The supplement contains enough vitamin C for consumption of from 100 milligrams to 5 grams thereof per 120 pounds of body weight per day, or vitamin E for consumption of from 30 milligrams to 2 grams thereof per 120 pounds of body weight per day, or the other edible natural antioxidants for consumption of from 10 milligrams to 1 gram thereof per 120 pounds of body weight per day, or of the edible synthetic antioxidant for consumption of from 0.01 to 500 milligrams thereof per 120 pounds of body weight per day, or mixtures (combination thereof).

The supplement is preferably contained in capsules, tablets or pills. If the resulting capsule is too large for ingestion by man and/or animal, the daily unit dosage of course can be placed in more than one capsule, all to be consumed daily so that the daily unit dosage is received.

This invention also includes the process of preparing the food and feed supplement of this invention. The process preferably involves placing the supplement in capsules, for daily unit dosages.

The term "edible" is defined herein as not possessing long term toxic effects in man and/or animal.

I have found that certain combinations and certain quantity ranges of free-radical inhibitors have other valuable effects in addition to retarding senescence. Inhibition of free radicals has been described as delaying the ageing process by reducing liquid peroxidation and random free-radical attacks on DNA, RNA, RNA sythetase, structural protein and cellular membranes. A combination of antioxidants was stressed to provide immediate scavenging of free radicals whether they be in aqueous or liquid media. Certain ingredients of those formulations are believed to play additional roles deside antioxidant, free-radical scavenger or radiation protector.

In addition to noting a retardation of the ageing process, I have observed increased lifespans in experimental animals. The increased lifespan has been primarily due to retarding the deleterious effects of ageing. However, the prevention of disease has contributed to increased lifespan.

The absence of cancer and gross tumors in the test animals has been striking in comparison to the controls and what is normally experienced.

The disease prevention has been primarily brought about by preventing carcinogenic materials from exciting viral genomes by free-radical reactions. A secondary mechanism is the preservation of membrane surface integrity, especially in regard to topography. Free-radical attack at the membrane surface could form topographical "holes" or "gaps" in the distribution of electronic charges, resulting in abnormal cellular chemistry.

The role of food and feed supplements and formulations has been described in retarding senescence, protecting against oxidizing air pollutants, and protecting against radiation. Cancer in man and/or animal can be reduced or prevented by the same formulations and the additional formulations described herein.

Known carcinogenic substances predictably produce certain types of cancers. The formulations of this invention prevent or reduce the incidence of these cancers whether in or on the stomach, breast, bladder, lung, colon, or other organs, or skin or other non-cutaneous portions of the body. The carcinogens are free-radical producers that either destroy membrane topography themselves or activate viral genomes which destroy membrane topography. The formulations of this invention interfere with such process of membrane topography destruction.

The fact that a non-carcinogenic compound can be converted into a carcinogen is illustrated by 3-hydroxyanthranilic acid (a metabolic intermediate of tryptophan, also called 3-hydroxyanthranilate) which can be readily converted to cinnibaric acid in urine both in vitro and in vivo. The addition of antioxidants and free-radical scavengers to the urine interfere with the conversion of 3-hydroxyanthranilic acid to cinnabaric acid and interferes with the free-radical propagating activity of cinnabaric acid. A water-soluble antioxidant (such as ascorbic acid) alone could preclude the formation of cinnabaric acid, but more complete protection requires a sulfhydryl group from a sulfur containing ingredient such as an edible sulfur-contain-

ing amino acid. The sulfhydryl group catalyses the metabolic oxidation of 3-hydroxy-anthranilic acid to α-amino β-carboxy-muconic acid, thus removing it from possibly converting to the carcinogen, i.e., cinnabaric acid. (See p. 365 of Harper's Review of Physiological Chemistry, 12th Ed. L. M. Pub, Los Altos, Calif.) The high incidence of bladder cancer in heavy smokers can be explained by the fact that their urine is deficient in ascorbic acid, high in cinnabaric acid, and high in free-radicals and chemilumenscence which probably consumes any naturally occurring free-radical scavengers normally present in the urine.

Free-radicals are in greater concentration in cancers of the liver, uterus, skin and stomach. Protection by a combination of compounds, with one or more present in each aqueous or lipid media, and in body pools, the bladder, and the colon, can concurrently protect against the formation of all types of cancer.

Skin cancer caused by extreme ultraviolet radiation exposure, long heat exposure, nuclear radiation or painting with a carcinogen can be prevented by skin application of the formulations of this invention, or by ingestion of the formulations of this invention. Stomach cancer caused by the ingestion of the carcinogen DMBA (7,12-dimethyl-benz-(a) anthracene) can be prevented by first injecting the food and supplements of this invention.

One of the chemical ingredients of this invention by itself will not offer the complete protection provided by the combination. One ingredient may prevent a specific cancer from forming, but only because it has altered the mechanism so that cancer appears elsewhere (probably because the other organ is not protecteed by the ingredient). It is important to first saturate the entire body system with the ingredients of this invention, then continued usage of the ingredients of this invention offers maximum protection against the occurrence of cancer. (The supplement of this invention offers far better protection against the occurrence of cancer than known or suggested means and for better retardation of cancer than known or suggested means.)

This invention also protects against radiation damage by increasing the body's tolerance to radiation and efficiency in utilizing oxygen.

The supplement of this invention protects against cancer caused by air pollutants such as 3,4-benzpyrene and di-alkylated benz(c) acridines.

The fool and feed supplements of this invention include edible sulfur-containing amino acids, proteins, peptides or mixtures thereof. The edible sulfur-containing ingredient is used in an amount from 100 milligrams to 2 grams per 120 pounds of body weight per day and preferably from 200 to 400 milligrams per 120 pounds of body weight per day.

Sulfur-containing amino acids, peptides and proteins protect against carcinogens in the digestive tract, e.g., in the stomach by chemically tying up the carcinogens or catalysing normal metabolism. Sulfur amino acids can add to the ring structure of the carcinogen, thus altering the K-region and destroying the coplanar molecular conformation and optimum incumbrance area required for carcinogenic activity. This is an example of the action of the sulfur-containing ingredient within the scope of this invention.

Examples of useful edible sulfur-containing amino acids are: cysteine (preferred), 2-amino - 4,4 - dimethyl - mercaptobutyric acid, methionine, cystine, djenkolic acid, 2-amino - 4 - isopropyl - mercaptobutyric acid, 2 - amino - 4 - butyl - mercaptobutyric acid, 2 - amino - 4,4 - diethyl - mercaptobutyric acid, dibenzoyldjenkolic acid, the monohydrochloride of djenkolic acid, the hydrochloride of cystine, 2 - amino - 2 - ethyl - 3 - mercaptopropanoic acid, the hydrochloride of cysteine, homocysteine, pantethene, the hydrochloride of cysteine and cysteic acid. All isomeric forms can be used.

The sulfur-containing amino acids, proteins, and peptides are normally used in the hydrochloride form or in weak acid or base salt form because they are more readily water soluble.

Peptides contain two or more amino acids held by the amido linkage

$$—NH—CO—$$

or

$$—N=C(OH)—.$$

Examples of useful edible sulfur-containing peptides are: glutathione (a tripeptide of glutamic acid, cysteine and glycine, also termed gamma - glutanyl - cysteinyl - glycine), cysteinyl-glycine, and gamma-cysteinyl-methionyl-glycine.

Examples of useful edible sulfur-containing proteins are: keratin, insulin, albumin, ribonuclease, fibroin, collagen and elastin. All of the scleroproteins (albuminoids), some of which are mentioned above, are useful.

The food and feed supplements of this invention include edible antioxidants. The edible antioxidant is used in an amount set forth elsewhere in this application.

The edible antioxidants, among other things, break free radical chains, quench electron mobility and scavenge for free radicals. In vivo, antioxidants act to decrease lipoxidase (an enzyme that produces in vivo auto-oxidation by initiating free radical chain reactions) capacity by donating electrons or hydrogen radicals to the enzyme, by pro-

tonating peroxide-free liquid free radicals on the enzyme surface or by inhibiting free radical formation.

Vitamin C is an edible antioxidant, even though it also is a membrane stabilizer. Vitamin C is L-ascorbic acid. Ascorbic acid is water soluble and is in the solid state at room temperature (melting point =190—192°C.). The non-toxic salts, esters and derivatives of vitamin C can also be used and are edible antioxidants. Vitamin C forms stable metal salts, such as sodium ascorbate, which can be used. Sodium ascorbate can be formed by the method described in U.S. Patent No. 2,442,005. 120 mg. of sodium ascorbate are equivalent in vitamin C activity to 100 mg. of ascorbic acid. Sodium ascorbate is water soluble and is a solid at room temperature. Ascorbyl palmitate can be used. Of all of the antioxidants, vitamin C is preferred.

Vitamin C, for example, blocks the conversion of some compounds into carcinogens in the stomach and the rest of the digestive tract.

The supplement contains enough vitamin C, when it is used as the antioxidant, for consumption of from 100 milligrams to 5 grams thereof preferably 250 milligrams to 2 grams, in a daily unit dosage.

Edible antioxidants, as used herein, includes edible lipid antioxidants.

The supplement contains enough edible synthetic lipid antioxidants, when it is used, for consumption of from 0.01 to 500 milligrams thereof preferably from 10 to 100 milligrams in a daily unit dosage.

Examples of useful edible synthetic lipid antioxidants are: butylated hydroxytoluene (BHT) (preferred), butylated hydroxyanisole (BHA), 2 - mercaptomethyl - amine, N,N'diphenyl - p - phenylenediamine, ammonium diethyldithiocarbamate, 1,2 - dihydro - 6ethoxy - 2,2,4 - trimethylquinoline (ethoxyquin), amino ethyl isothyromium, aromatic phenols, aromatic amines, oxalic acid, cephalin, methylene blue, nordehydroquaretic acid, propylgallate, gallic acid, hydroxy urea, oxophenarsine, citric acid, 4 - methyl - 2,6di - tert. - butyl - phenol, phytylubichromel, methyl glyoxal, hydroquinone, di - tert. - amylhydroquinone, o-, m- or p- benzoquinone, and py-gol.

The supplement contains enough edible natural lipid antioxidant when it is used, for consumption of from 10 milligrams to 1 gram thereof preferably from 100 to 500 milligrams in a daily unit dosage.

Examples of useful edible natural lipid antioxidants are ubiquinone and vitamin K. Some of the natural antioxidants may be prepared synthetically, but they are treated herein as natural antioxidants. A useful edible natural antioxidant is 2,3 - dimethoxy - 5 - methylbenzoquinones having polyisoprenoid side chains at the number six carbon.

Vitamin E is a natural antioxidant but its usage, amount differs. The supplement contains enough vitamin E, when it is used, for consumption of from 30 milligrams to 2 grams thereof preferably 250 milligrams to 1 gram in a daily unit dosage.

The vitamin E component may be present as a pure compound, preferably alpha-tocopherol, but can be β-tocopherol, delta-tocopherol or gamma-tocopherol. The vitamin E component may also be present as active compounds thereof, for example, the acetate, succinate and other esters. Compounds, such as, tocopherylquinone, can be used. Any of the active isomeric forms including the dl- and l- forms of the compounds mentioned may be used as many natural materials and extracts having Vitamin E activity. (There is no theoretical upper limit to the amount of Vitamin E used since the body excretes or stores all excess amounts.)

Vitamin E is known as a lipid antioxidant and in the body reduces the biological need for oxygen. This vitamin increases the efficiency of oxygen transfer in the body and also reduces the amount of free oxygen stored therein since it will preferentially react with free oxygen before the various body components. Thus, Vitamin E may said to "preserve" such body components as red blood cells and arterial wall lipids by preferentially reacting with free oxygen or other oxidizing substances which would otherwise attack the body components. Most important and critical from a standpoint of the present invention it has been shown that Vitamin E exhibits a unique and vital synergistic effect with the selenium-organic complex known as Factor 3.

The Vitamin E may conveniently be added in admixture with a vegetable oil, and particularly with a seed germ oil such as wheat germ oil, safflower oil, corn oil and soybean oil.

The food and feed supplements of this invention include selenium. The selenium can be present as the oxide or as an organic selenium compound. The selenium, measured as oxide, is used in an amount from 0.01 to 100 milligrams per 120 pounds of body weight per day and preferably from 1 to 10 milligrams per 120 pounds of body weight per day.

Selenium occurs naturally in varying amounts in a wide variety of foods and also is normally present as an impurity in the edible sulfur-containing amino acids, e.g., in methionine as the compound selenomethionine. This later is due to the fact that the chemical behavior and reactivity of sulfur and selenium are so similar that it is extremely difficult if not impossible to completely remove selenium from sulfur-containing compounds. Thus, in food grade or edible sulfur-containing amino acids, the corresponding seleno-amino acid is normally present and

thus contains selenium in amounts within the above range. For example, one gram of a commercial food grade sample of cysteine was analyzed in the prior art, and found to contain about 75 weight percent (750 milligrams) of the cysteine and contained about 0.1 weight percent (1 milligram) selenocysteine which was roasted to an ash containing about 0.65 milligrams of selenium, as oxide. Even in research grade sulfur-containing amino acids, some small amounts of the seleno form are unavoidably contained therein.

Examples of useful edible selenium compounds are selenomethionine, the selenium oxides, and selenoglutathione, selenocystine.

The food and feed supplements of this invention may include membrane stabilizers such as antihistamines (e.g. pheniramine maleate), salicylates (e.g., acetylsalicylic acid) and corticosteroids (e.g., cortisone).

Other nutrients, fillers, vitamins, can be added to the food and feed supplements of this invention.

All of the range amounts of ingredients set forth herein are based on the active component, so salts, etc., thereof may have to be used in correspondingly larger amounts.

This invention is useful in the treatment of man and animal.

The following specific examples are indicative of optimum and preferred food and feed supplement formulations in accordance with the present invention. In each case, the mixture was prepared and placed in one or more size 0 or larger gelatin capsules depending upon the final bulk of the mixture (Capsule series of "The Pharmacopeia of the United States", 15th Revision.) In all of the examples, the sulfur-containing amino acid was research grade, unless otherwise specified. In all of the examples, unless otherwise specified, parts, ratios and percentages are by weight.

EXAMPLE

3 grams of glutathione, 10 grams of ascorbic acid, 10 grams of Alpha tocopherol, and 1 gram of butylated hydroxytoluene were mixed. The mixture was divided into 10 equal portions and transferred into gelatin capsules. Each completed capsule contained 0.3 gram of glutathione, 1 gram of ascorbic acid, 1 gram of alpha tocopherol, 5 milligrams of selenium (as oxide) and 0.1 gram of butylated hydroxytoluene. A completed capsule was taken each day by an adult human.

This invention also encompasses the feed and feed supplement containing as essential ingredients (a) a sulfur-containing amino acid, (b) an edible selenium compound and (c) an antioxidant selected from vitamin E and a mixture of vitamin E with a synthetic lipid antioxidant. Such a food and feed supplement (i) is effective in retarding or delaying a substantial portion of the biological degradation normally associated with the ageing process, (ii) will retard degradation of RNA synthesis, prevent the accumulation of mis-synthesized RNA cells and protein in the body and reduce the antibody reaction thereto, (iii) are effective in combating the ageing acceleration effects of stress and stress related factors, (iv) are effective in reducing and/or delaying the accumulation of lipofuscin or age pigment in ageing body cells, (v) increase the body's tolerance to radiation and efficiency in utilizing oxygen, (vi) aid in establishing and maintaining proper protein synthesis in the body which combat both improper nitrogen balance and poor tissue replacement, and (vii) inhibit free radical reactions in the body and help rid the body of free radicals produced.

This invention further encompasses the food and feed supplement which contains four critical ingredients, namely, an antioxidant selected from vitamin E and mixtures thereof with a synthetic lipid antioxidant, the trace element selenium, a sulfur-containing amino acid, and vitamin C (which is a membrane stabilizer and an edible antioxidant). Such a food and feed supplement protests cell membranes from breakdown resulting from free radical attack on the cells.

Agents or compounds which protect cell membranes resulting from breakdown resulting from free radical attack on the cells are the membrane stabilizers. A membrane stabilizers, such as vitamin C protects the cells from free radical attack which would otherwise lead to membrane breakdown and would mean a subsequent leakage of lysomal enzymes that also damage the DNA molecule. Broadly from 50 mg. to 0.5 gm. per 120 pounds of body weight of vitamin C should be consumed each day.

All of the above objects are attained by the use of the food and feed supplement which contains the five ingredients, namely, Vitamin E, Vitamin C, a synthetic lipid antioxidant, the trace element selenium in edible form and a sulfur-containing amino acid.

WHAT I CLAIM IS:—

1. A food and feed supplement containing as essential ingredients (a) edible selenium, as a selenium oxide or an organic selenium compound, (b) an edible antioxidant selected from vitamin C, vitamin E, other edible natural antioxidants, edible synthetic antioxidants and mixtures thereof, and (c) an edible sulfur-containing amino acid, an edible sulfur-containing protein, an edible sulfur-containing peptide or mixtures thereof, said edible sulfur-containing amino acid, protein or peptide not being an edible antioxidant, said food and feed supplement being in a daily unit form containing from 100 milligrams to 2 grams of said sulfur-containing amino acid, protein, peptide or mixtures

thereof, from 0.01 to 100 milligrams, calculated as SeO_2, of said edible selenium and from 100 milligrams to 5 grams of said vitamin C, or from 30 milligrams to 2 grams vitamin E, or from 10 milligrams to 1 gram of at least one of said other edible natural antioxidants, or from 0.01 to 500 milligrams of at least one of said edible synthetic antioxidant or mixtures thereof.

2. A food supplement as described in Claim 1 wherein the sulfur-containing amino acid is selected from cysteine, cystine, djenkolic acid and methionine.

3. A food and feed supplement as described in Claim 1 wherein said daily dosage unit contains said edible sulfur-containing amino acid, peptide or protein in an amount from 200 to 400 milligrams.

4. A food supplement as described in Claim 1 wherein said edible synthetic antioxidant is selected from butylated hydroxytoluene, butylated hydroxyanisole, 2 - mercaptomethylamine, N,N' - diphenyl - p - phenylenediamine, ammonium diethyldithiocarbamate, 1,2-dihydro - 6 - ethoxy - 2,2,4 - trimethylquinoline, amino ethyl isothyromium, aromatic phenols ,and aromatic amines.

5. A food and feed supplement as described in Claim 1 wherein vitamin C is present and said daily unit dosage contains from 250 milligrams to 2 grams of said vitamin C.

6. A food supplement as described in Claim 1 wherein said antioxidant is vitamin C.

7. A food supplement as described in Claim 6 wherein said vitamin C is selected from L-ascorbic acid, sodium ascorbate and ascorbyl palmitate.

8. A food and feed supplement as described in Claim 1 wherein vitamin E is present and said daily unit dosage contains from 250 milligrams to 1 gram of vitamin E.

9. A food and feed supplement as described in Claim 1 wherein said edible synthetic antioxidant is present and said daily unit dosage contains from 10 to 100 milligrams of said edible synthetic antioxidant.

10. A food and feed supplement as described in Claim 1 wherein said edible natural antioxidant is present and said daily unit dosage contains from 100 to 500 milligrams of said edible natural antioxidant.

11. A food and feed supplement as described in Claim 1 wherein said food and feed supplement is contained in at least one capsule, pill or tablet.

12. A food and feed supplement as claimed in Claim 1, substantially as hereinbefore described.

13. A food and feed supplement according to Claim 1 substantially as described in the example.

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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1976.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.